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Via Hand Delivery

February 7, 2000

Dockets Management Branch
Food and Drug Administration
5630 Fishers Lane
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Re: Draft Guidance for Industry on Applications Covered by Section 505(b)(2), Docket No. 99D-4809

Dear Sir or Madam:

Pfizer Inc. hereby submits the attached comments on the draft guidance made available by the Food and Drug Administration on December 8, 1999, concerning new drug applications covered by section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act.

Sincerely yours,

Rudy A. Johnson

99D-4809

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Comments to the Food and Drug Administration Regarding Drug Approvals Under Section 505(b)(2)

Pfizer submits these comments to the Food and Drug Administration's (FDA) draft guidance on new drug applications (NDAs) covered by section 505(b)(2) of the Food, Drug, and Cosmetic Act (the Act) (the draft Guidance Document)[1] Pfizer objects to those parts of the draft Guidance Document that assert FDA's authority to approve new drug applications that rely on a prior Agency finding of safety and efficacy. For the reasons set forth below, Pfizer requests that FDA withdraw and reissue the draft Guidance Document to make clear that the Agency will not approve under section 505(b)(2) of the Federal Food Drug and Cosmetic Act a new drug application (NDA) that relies on a prior finding of safety and efficacy. To the extent that the draft Guidance Document reflects FDA's interpretation of 21 C.F.R. § 314.54, Pfizer also requests that FDA initiate rulemaking to modify that regulation in a similar manner.

Pfizer's objections are as follows. First, reliance on, or the unauthorized use of, an innovator's safety and efficacy data to approve a competitor's NDA is not supported by any reasonable construction of the Act, and conflicts with other statutory protections relating to the use of proprietary data.[2]

Second, the Act does not permit the Agency to apply a less rigorous safety and efficacy standard to a 505(b)(2) application than to a 505(b)(1) application.

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1 Guidance for Industry: Applications Covered by Section 505(b)(2), Draft Guidance, Food and Drug Administration, Center for Drug Evaluation and Research (CDER), October 1999.

2 See e.g., 18 U.S.C. 1905 (Trade Secrets Act); 21 U.S.C. 331(j) (FFDCA prohibition against FDA disclosure of trade secret information)

Third, the reliance by FDA or an applicant on the Agency's prior finding of the safety and efficacy to approve a 505(b)(2) application constitutes an unconstitutional taking and, thus, is unlawful.

Accordingly, FDA may not implement the draft Guidance Document or rely on 21 C.F.R. § 314.54 to approve an application that is based on a prior finding of safety and efficacy for an innovator's drug product under section 505(b)(2) of the Act and must require such applications to be supported by the same scope of data necessary to support a 505(b)(1) application.

I. Section 505(b)(2) Does Not Authorize FDA to Approve a New Drug Application Based On the Agency's Prior Finding of Safety and Efficacy

In FDA's draft Guidance Document, the Agency has stated that it will accept and approve 505(b)(2) applications for new drug products that rely on "the Agency's finding of safety and effectiveness for an approved drug, without regard to a right to rely on such data."[3] See Guidance Document, at 2. In essence, therefore, the Agency intends to rely on the unauthorized use of an innovator's proprietary and commercially valuable safety and efficacy data to approve another company's drug product under section 505(b)(2) of the Act.[4] A proper construction of section 505(b)(2), consistent with the Hatch-Waxman Amendments, the legislative history of the Act, and other statutory protections for the proper and legal use of proprietary safety and effectiveness data,[5] however, do not support FDA's expansion of section 505(b)(2) to approve applications that rely on the use of an innovator's proprietary data without the innovator's authorization.

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3 Pfizer notes that FDA's recently articulated policy is the first formal declaration by FDA of the Agency's intention to permit a 505(b)(2) applicant to rely primarily on a prior finding of safety and effectiveness based on the unauthorized use of an innovator's data. See 21 C.F.R. § 314.54(a)(1)(iii) (no statement that FDA intends to allow the unauthorized use of prior finding of safety and efficacy). In addition, even if the FDA's actions were authorized by the Act, the Agency may not issue such a substantive change in policy in a Guidance Document, but must issue it as a rulemaking subject to notice and comment.

4 See Guidance Document, at 2 noting that the Agency will accept:

The Hatch-Waxman Amendments added section 505(b)(2) to the Act to codify FDA's "paper NDA" policy which permitted an applicant to submit published literature to support the safety and efficacy of a duplicate of a drug product that was first approved for marketing after 1962.[6] The provision, therefore, was intended to allow an applicant to substitute literature to satisfy the "full reports" requirements of section 505 (b)(1) of the Act. See H.R. 98-857, Part I, 98th Cong. 2d. Sess. 36 *reprinted in* 1984 U.S. Code Cong. Admin. News 2647, 2649 (stating that "under the Paper NDA procedure, the generic manufacturer may submit scientific reports, instead of clinical trials, to support findings of safety and efficacy."). In fact, the Agency itself has recognized that the Act does not authorize the approval of 505(b)(2) applications based on an innovator's safety and effectiveness data. See 54 Fed. Reg. 28872, 28892 (July 10, 1989) (Agency recognition of the failure of the Hatch-Waxman Amendments to directly address the appropriate mechanism for obtaining approval of a significant product change that requires the review of clinical investigations and, therefore, is ineligible for approval under the 505(j) Abbreviated New Drug Application ("ANDA") mechanism.); see also 54 Fed. Reg. at 28875 (July 10, 1989) (recognizing that the term "paper NDA," as it was used when Congress passed the Hatch-Waxman Amendments, was defined and understood to encompass only applications for duplicate copies of drugs first approved after 1962 that met the "full reports requirements" of section 505(b)(1) of the Act through published reports in the medical literature establishing the drug's safety and effectiveness). Accordingly, FDA's proposed approval of this broad category of 505(b)(2) applications exceeds the Agency's statutory authority and, thus, is unlawful.

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a 505 (b)(2) application for a change in a drug when approval of the application relies on the Agency's previous finding of safety and/or effectiveness for a drug. This mechanism, which is embodied in a regulation . . . , essentially makes the Agency's conclusions that would support the approval of a 505 (j) application available to an applicant who develops a modification of a drug).

5 See e.g., 18 U.S.C. § 1905, 21 U.S.C. § 331(j).

6 The policy was limited to copies of drug products (or closely related forms) marketed after 1962 and offered for the same indications.

If Congress had intended for the Agency to approve applications under section 505(b)(2) of the Act as suggested in the draft Guidance Document, Congress would have included express language in that section, similar to the language included in section 505(j) of the Act, which allows an applicant to show that an unapproved drug product is the same as a previously approved drug product ("a listed drug product") and, thus, expressly authorizes the Agency to approve the generic drug based on a finding of safety and efficacy of an innovator's product. See 21 U.S.C. 355(j). Nothing in the Act, however, suggests that Congress intended to allow such approvals under section 505(b)(2). To allow the blurring of these two different mechanisms is to undermine the statutory framework of the Act and the deliberate differences which Congress expressly intended for drug approvals.

II. FDA's Proposed Reliance on Prior Findings of Safety and Efficacy Violates the Act by Allowing Approval of 505(b)(2) Applications Based on a Less Rigorous Showing of Safety and Efficacy than 505(b)(1) Applications

FDA's proposal to rely on prior findings of safety and efficacy would also violate the Act because it would allow the Agency to approve drug products that differ significantly from a listed drug product but that do not include the same scope of safety and efficacy data required for 505(b)(1) applications. Specifically, FDA's draft Guidance Document allows the Agency to approve drugs that differ significantly from a listed drug under section 505(b)(2) of the Act based on: (1) data on which neither the applicant nor the FDA has the right to rely; or alternatively (2) incomplete data not consisting of "full reports." Reliance on incomplete data would result in a less rigorous showing of safety and effectiveness under section 505(b)(2) than that required of applications that are submitted under section 505(b)(1) of the Act. See e.g. draft Guidance Document at 8 (stating that the Agency will accept 505(b)(2) applications for drug products that are different from a listed drug, that rely on the Agency's prior finding of safety and effectiveness of the listed drug and less than complete studies of safety and effectiveness ("bridging studies") to "provide an adequate basis for reliance upon [such a] finding").

Even the Agency has recognized that the scope of evidence demonstrating safety and efficacy are the same under section 505(b)(2). See, e.g., 21 C.F.R. 314.50(d)(2). (5), (6) (requiring reports of nonclinical pharmacological and toxicological studies, clinical data, and statistical data for both 505(b)(1) and (b)(2) applications); see 54 Fed. Reg. 28872, 28875, 28892 (July 10, 1989) (noting that applications that meet the description in section 505(b)(2) of the Act are subject to the same provisions that govern a full NDA). Section 505(b) requires both 505(b)(1) and 505(b)(2) applications to include: "full reports of investigations which have been made to show whether or not such drug is safe for use and whether such drug is effective in use" as described in section 505(b)(1)(A). Congress recognized that some of the critical data to support safety and efficacy may be found in studies not conducted by or for the applicant. Section 505(b)(2) allows an applicant to rely on such studies if they are in the public domain e.g., "published reports." 21 U.S.C. 355(b)(1), (b)(2). Nothing in the statute indicates that Congress intended to lessen the safety and efficacy showing for a 505(b)(2) application.

Moreover, Congress made clear that where it did intend to allow reliance on FDA's prior findings of safety and efficacy such as under section 505(j), it intended to allow such drugs to differ only in limited ways from the listed product. Under section 505(j), these specific limits include variations in route of administration, dosage form, strength, or where one of the active ingredients differs from those in the listed drug that is also a combination drug, without having to regenerate full reports of safety and efficacy. Id. See H.R. Rep. 9 -857, Part I, 98th Congress, 2d Sess. 36, *reprinted in* 1984 U.S. Code. Cong. Admin. News 2656 (stating that an applicant may petition for approval of a drug product that varies from the listed drug in route of administration, dosage form, strength, or where one of the active ingredients differs from those in a listed drug that is also a combination drug, and that "these are the only changes that are permitted").

To the extent, therefore, that the Agency relies on the draft Guidance Document and 21 C.F.R. 314.54 to approve 505(b)(2) applications for drug products that include other more

significant differences from the listed drug, and are based only on incomplete studies, i.e., limited bridging studies, the draft Guidance Document and regulation are illegal.

III. The Approval of a 505(b)(2) Application Based on FDA's Prior Finding of Safety and Efficacy Constitutes an Unconstitutional Taking

Finally, the Agency's proposed unauthorized use of an innovator's data is unsupported by the statute and legislative history, is fundamentally unfair to research-based companies, and constitutes an unconstitutional taking. Under the Fifth Amendment of the United States Constitution, the government may not appropriate another's property without just compensation. In its draft Guidance Document, however, FDA has stated that it will allow an applicant to rely without authorization on an innovator's property in direct contravention of these constitutional protections.

The inherent property right in safety and efficacy data that is submitted as part of an NDA has been historically recognized by the Courts, Congress, and the Agency. The courts, for example, have noted that safety data is property and, thus, protected by the Fifth Amendment. See Ruckelshaus v. Monsanto Co, 467 U.S. 986 (1984) (recognizing the inherent property right of safety data contained in applications for registration of pesticides to approve generic copies of previously approved pesticides under the Federal Insecticide, Fungicide, and Rodenticide Act ("FIFRA"); see also Tri-Bio Laboratories, Inc. v. United States, 836 F.2d 135 (3d. Cir. 1987), *cert denied*, 484 U.S. 818 (1988) (recognizing that approval of a generic animal drug based on an innovator's ANADA is a taking of the innovator's rights in the data.). In addition, Congress also has acknowledged the inherent property rights in such information in several statutes, including the Trade Secrets Act, (18 U.S.C. 1905) and at 21 U.S.C. 331(j).

Moreover, the Agency has recognized the inherent and protected rights in such information. See e.g., 21 C.F.R. 314.50 (g) (FDA recognition of the inherent property right of clinical and other NDA data as trade secret and, thus, recognizing it as protected from public dissemination/disclosure by requiring an application that contains "a reference to information submitted to the agency by a person other than the applicant . . . to contain a written statement that authorizes the reference and that is signed by the person who submitted the information."); 39 Fed. Reg. 44635 (Dec. 24, 1974) (recognizing trade secret status of safety and effectiveness data in an NDA as a property right and the right to charge a competitor for reference to that data if the competitor wishes to obtain approval of a generic copy of the product); see also 46 Fed. Reg. 27396 (May 10, 1981) ("the Finkel Memorandum") (stating that "no data in an NDA can be utilized to support another NDA without express permission of the original NDA holder" and thus, stating that for "duplicate NDAs for already approved post [19]62 drugs, the Agency will accept published reports as the main supporting documentation for safety and effectiveness."). As such, the Agency may not implement or rely on the draft Guidance Document or 505(b)(2) regulation to the extent that it would permit FDA to rely on a finding of safety and efficacy of an innovator's drug product without authorization and thereby illegally appropriate the commercial value of that data.

IV. Conclusion

The Act is clear that FDA must require the same scope and quality of evidence of safety and efficacy for a drug approval under 505(b)(2) as that required under 505(b)(1). Nothing in the Act allows FDA to short circuit that requirement by illegally relying on data and prior findings of safety and efficacy which it has no right to divulge or reference. For the foregoing reasons, therefore, and to avoid engaging further in illegal and improper action that will significantly adversely affect research-based companies, the FDA should withdraw and/or reissue the 505(b)(2) draft Guidance Document and should not apply 21 C.F.R. §314.54 to approve NDAs that rely without authorization on proprietary data.

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Number of Pages (INCLUDING COVER PAGE): 9

Note:

Comments:

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